

IPW

AUG 30 2004

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Phillips *et al.* Confirmation No.: 1302
 Appl. No.: 10/755,545 Group Art Unit: 1646
 Filed: 1/12/04 Examiner: To be Assigned
 For: COMPOSITIONS AND METHODS FOR THE TREATMENT OF DISEASE

Mail Stop Amendment
 Commissioner for Patents
 P.O. Box 1450
 Alexandria, VA 22313-1450

**INFORMATION DISCLOSURE STATEMENT
 CITATION UNDER 37 C.F.R. § 1.97)**

Attached is a list of documents on form PTO-1449. Some of the documents listed on the attached PTO-1449 are cited herein because they were cited in the Search Report of corresponding International Application Number PCT/AU02/00945. The Search Report is enclosed.

In accordance with the Office waiver published July 11, 2003, copies of the cited U.S. patents and patent application publications are not enclosed. Applicant does enclose copies of any cited foreign patent documents and non-patent literature in accordance with 37 CFR 1.98(a)(2).

It is requested that the Examiner consider these documents and officially make them of record in accordance with the provisions of 37 C.F.R. § 1.97 and Section 609 of the MPEP. By submitting the listed documents, Applicant in no way makes any admission as to the prior art status of the listed documents, but is instead submitting the listed documents for the sake of full disclosure.

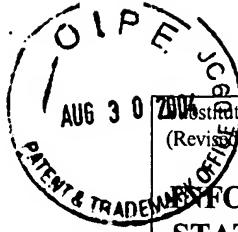
Respectfully submitted,

Kelly J. Williamson

Patent Agent

Registration No. 47,179

<p>CUSTOMER NO. 00826 ALSTON & BIRD LLP Bank of America Plaza 101 South Tryon Street, Suite 4000 Charlotte, NC 28280-4000 Tel Raleigh Office (919) 862-2200 Fax Raleigh Office (919) 862-2260</p>	<p>CERTIFICATE OF MAILING</p> <p>I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on August 27, 2004</p> <p></p> <p>Pamela Lockley</p>
--	--



AUG 3 0 2004
Complete if Known
(Revised 04/2003)

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Use as many sheets as necessary)

Sheet	1	of	7	Attorney Docket Number	048501/273281
-------	---	----	---	------------------------	---------------

U. S. PATENT DOCUMENTS

Examiner Initials*	Cite No.	Document Number Number - Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages of Relevant Figures Appear

FOREIGN PATENT DOCUMENTS

Examiner Initials	Cite No.	Foreign Patent Document Country Code - Number Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	English Language Translation Attached
1	WO 96/11259		04-18-1996	HE <i>et al.</i>		
2	WO 99/10364		03-04-1999	RUBEN <i>et al.</i>		

OTHER DOCUMENTS

Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s) , volume-issue number(s), publisher, city and/or country where published.	English Language Translation Attached
	3	ALCOLADO, R., <i>et al.</i> , "Pathogenesis of live fibrosis," <i>Clin. Sci. (Colch.)</i> , 1997, pp. 103-112, Vol. 92(2).	
	4	ARTHUR, M., "Fibrogenesis: Metalloproteinases and their inhibitors in liver fibrosis," <i>American Journal of Physiology – Gastrointestinal and Liver Physiology</i> , 2000, pp. G245-G249, Vol. 279.	
	5	DATE, M., <i>et al.</i> , "Differential expression of transforming growth factor β and its receptors in hepatocytes and nonparenchymal cells of rat liver after CCl ₄ administration," <i>Journal of Hepatology</i> , 1998, pp. 572-581, Vol. 28.	
	6	DATE, M., <i>et al.</i> , "Differential regulation of activin A for hepatocyte growth and fibronectin synthesis in rat liver injury," <i>J Hepatol.</i> , 2000, pp. 251-260, Vol. 32(2).	
	7	DE BLESER, P.J., <i>et al.</i> , "Localization and cellular sources of activins in normal and fibrotic rat liver," <i>Hepatology</i> , 1997, pp. 905-912, Vol. 26(4).	
	8	DOOLEY, S., <i>et al.</i> , "Expression of Smads during <i>in vitro</i> transdifferentiation of hepatic stellate cells to myofibroblasts," <i>Biochem. Biophys. Res. Comm.</i> , 2001, pp. 554-562, 283.	
	9	ENGELSE, M.A., <i>et al.</i> , "Human activin A is expressed in the atherosclerotic lesion and promotes the contractile phenotype of smooth muscle cells," <i>Circulation Research</i> , 1999, pp. 931-939, Vol. 85.	

Examiner Signature	Date Considered
--------------------	-----------------

*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Use as many sheets as necessary)

Sheet 2 of 7 Attorney Docket Number 048501/273281

Complete if Known

Application Number	10/755,545
Filing Date	1/12/04
First Named Inventor	Phillips
Group Art Unit	1646
Examiner Name	To Be Assigned

U. S. PATENT DOCUMENTS

10	FRIEDMAN, S.L., <i>et al.</i> , "Hepatic lipocytes: the principal collagen-producing cells of normal rat liver," <i>Proc. Natl. Acad. Sci. USA</i> , 1985, pp. 8681-8685, Vol. 82(24).
11	FRIEDMAN, S.L., <i>et al.</i> , "Modulation of transforming growth factor β receptors of rat lipocytes during the hepatic wound healing response. Enhanced binding and reduced gene expression accompany cellular activation in culture and <i>in vivo</i> ," <i>J. Biol. Chem.</i> , 1994, pp. 10551-10558, Vol. 269(14).
12	FRIEDMAN, S.L., <i>et al.</i> , "Molecular mechanisms of hepatic fibrosis and principles of therapy," <i>J. Gastroenterol.</i> , 1997, pp. 424-430, Vol. 32(3).
13	GEORGE, J., <i>et al.</i> , "In vivo inhibition of rat stellate cell activation by soluble transforming growth factor β type II receptor: A potential new therapy for hepatic fibrosis," <i>Proc. Natl. Acad. Sci. USA</i> , 1999, pp. 12719-12724, Vol. 96(22).
14	GRECO, B.A., <i>et al.</i> , "Atherosclerotic Ischemic Renal Disease," <i>Amer. J. Kidney Diseases</i> , 1997, pp. 167-187, Vol. 29(2).
15	HARADA, K., <i>et al.</i> , "Serum immunoreactive activin A levels in normal subjects and patients with various diseases," <i>J. Clin. Endocrinol. Metab.</i> , 1996, pp. 2125-2130, Vol. 81(6).
16	HUANG, X., <i>et al.</i> , "Expression changes of activin A in the development of hepatic fibrosis," <i>World Journal of Gastroenterology</i> , 2001, pp. 37-41, Vol. 7.
17	HÜBNER, G., <i>et al.</i> , "Activin A – a novel player and inflammatory marker in inflammatory bowel disease," <i>Lab. Invest.</i> , 1997, pp. 311-318, Vol. 77.
18	HÜBNER, G., <i>et al.</i> , "Strong induction of activin expression after injury suggests an important role of activin in wound repair," <i>Develop. Biology</i> , 1996, pp. 490-498, Vol. 173.
19	HULLY, J.R., <i>et al.</i> , "Induction of apoptosis in the murine liver with recombinant human activin A," <i>Hepatology</i> , 1994, pp. 854-862, Vol. 20.
20	ICHIKAWA, T., <i>et al.</i> , "Transforming growth factor β and activin tonically inhibit DNA synthesis in the rat liver," <i>Hepatology</i> , 2001, pp. 918-925, Vol. 34(5).
21	INOUE, S., <i>et al.</i> , "Expression of follistatin, an activin-binding protein, in vascular smooth muscle cells and arteriosclerotic lesions," <i>Arteriosclerosis and Thrombosis</i> , 1993, pp. 1859-1864, Vol. 13(12).
22	ISHAK, K., <i>et al.</i> , "Histological grading and staging of chronic hepatitis," <i>J. Hepatol.</i> , 1995, pp. 696-699, Vol. 22(6).

Examiner Signature	Date Considered
--------------------	-----------------

*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute for form 1449/PTO (Revised 04/2003)				Complete if Known	
				Application Number	10/755,545
				Filing Date	1/12/04
				First Named Inventor	Phillips
				Group Art Unit	1646
				Examiner Name	To Be Assigned
Sheet	3	of	7	Attorney Docket Number	048501/273281

U. S. PATENT DOCUMENTS

	23	ISSA, R., <i>et al.</i> , "Apoptosis of hepatic stellate cells: involvement in resolution of biliary fibrosis and regulation by soluble growth factors," <i>Gut</i> , 2001, pp. 548-557, Vol. 48(4).	
	24	KAY, M.A., <i>et al.</i> , "Liver regeneration: prospects for therapy based on new technologies," <i>Molecular Medicine Today</i> , 1997, pp. 108-115.	
	25	KOBAYASHI, T., <i>et al.</i> , "Expression of Inhibin β_A , β_B , and Follistatin mRNAs in the Carbon Tetrachloride Induced Rat Liver Regeneration Model," <i>Biol. Pharm. Bull.</i> , 2000, pp. 755-757, Vol. 23.	
	26	KOGAWA, K., <i>et al.</i> , "Immunohistochemical localization of follistatin in rat tissues," <i>Endocrinol. Japan</i> , 1991, pp. 383-391, Vol. 38(4).	
	27	KOGURE, K., <i>et al.</i> , "A single intraportal administration of follistatin accelerates liver regeneration in partially hepatectomized rats," <i>Gastroenterology</i> , 1995, pp. 1136-1142, Vol. 108(4).	
	28	KOGURE, K., <i>et al.</i> , "Immediate onset of DNA synthesis in remnant rat liver after 90% hepatectomy by an administration of follistatin," <i>J. Hepatol.</i> , 1998, pp. 977-984, Vol. 29(6).	
	29	KOGURE, K., <i>et al.</i> , "Intravenous administration of follistatin: delivery to the liver and effect on the liver regeneration after partial hepatectomy," <i>Hepatology</i> , 1996, pp. 361-366, Vol. 24(2).	
	30	KOGURE, K., <i>et al.</i> , "The role of activin and transforming growth factor- β in the regulation of organ mass in the rat liver," <i>Hepatology</i> , 2000, pp. 916-921, Vol. 31(4).	
	31	KOJIMA, I., <i>et al.</i> , "Role of the activin-follistatin system in the morphogenesis and regeneration of the renal tubules," <i>Molecular and Cellular Endocrinology</i> , 2001, pp. 179-182, Vol. 180.	
	32	KOTSUJI, T., <i>et al.</i> , "Effects of activin A on the growth of neurofibroma-derived cells from a patient with neurofibromatosis type 1," <i>Dermatology</i> , 2000, pp. 277, Vol. 201.	
	33	KOZAKI, K., <i>et al.</i> , "Activin/follistatin and atherosclerosis – A review," <i>J. Atherosclerosis and Thrombosis</i> , 1998, pp. 36-40, Vol. 5.	
	34	KOZIAN, D.H., <i>et al.</i> , "The activin-binding protein follistatin regulates autocrine endothelial cell activity and induces angiogenesis," <i>Lab. Invest.</i> , 1997, pp. 267-276, Vol. 76(2).	
	35	LAPING, N.J., "Therapeutic uses of smad protein inhibitors: selective inhibition of specific TGF- β activities," <i>IDrugs</i> , 1999, pp. 907-914, Vol. 2.	

Examiner Signature		Date Considered	
--------------------	--	-----------------	--

*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Use as many sheets as necessary)

Sheet

4

of

7

Complete if Known

Application Number	10/755,545
Filing Date	1/12/04
First Named Inventor	Phillips
Group Art Unit	1646
Examiner Name	To Be Assigned
Attorney Docket Number	048501/273281

U. S. PATENT DOCUMENTS

36	LEE, D.K., <i>et al.</i> , "The hepatitis B virus encoded oncoprotein pX amplifies TGF- β family signaling through direct interaction with Smad4: potential mechanism of hepatitis B virus-induced liver fibrosis," <i>Genes & Dev.</i> , 2001, pp. 455-466, Vol. 15(4).
37	MAESHIMA, A., <i>et al.</i> , "Hepatocyte growth factor induces branching tubulogenesis in MDCK cells by modulating the activin-follistatin system," <i>Kidney International</i> , 2000, pp. 1511-1522, Vol. 58.
38	MATSUDA, Y., <i>et al.</i> , "Preventative and therapeutic effects in rats of hepatocyte growth factor infusion on liver fibrosis/cirrhosis," <i>Hepatology</i> , 1997, pp. 81-89, Vol. 26(1).
39	MATSUSE, T., <i>et al.</i> , "Expression of immunoreactive activin A protein in remodelling lesions associated with interstitial pulmonary fibrosis," <i>Amer. J. Path.</i> , 1996, pp. 707-713, Vol. 148.
40	MATSUSE, T., <i>et al.</i> , "Expression of Immunoreactive and Bioactive Activin A Protein in Adult Murine Lung after Bleomycin Treatment," <i>Amer. Journal of Respiratory Cell and Molecular Biology</i> , 1995, pp. 17-24, Vol. 13(1).
41	MICHALOPOULOS, G. K., <i>et al.</i> , "Liver Regeneration," <i>Science</i> , 1997, pp. 60-66, Vol. 276.
42	MOLLOY, C.J., <i>et al.</i> , "Novel cardiovascular actions of the activins," <i>J. Endocrin.</i> , 1999, pp. 179-185, Vol. 161.
43	MUNZ, B., <i>et al.</i> , "A novel role of activin in inflammation and repair," <i>J. Endocrin.</i> , 1999, pp. 187-193, Vol. 161.
44	NAKAMURA, T., <i>et al.</i> , "Inhibition of transforming growth factor β prevents progression of liver fibrosis and enhances hepatocyte regeneration in dimethylnitrosamine-treated rats," <i>Hepatology</i> , 2000, pp. 247-255, Vol. 32(2).
45	NIETO, N., <i>et al.</i> , "CYP2E1-mediated oxidative stress induces collagen type I expression in rat hepatic stellate cells," <i>Hepatology</i> , 1999, pp. 987-996, Vol. 30(4).
46	OGAWA, K., <i>et al.</i> , "Activin A stimulates type IV collagenase (matrix metalloproteinase-2) production in mouse peritoneal macrophages," <i>J. Immunol.</i> , 2000, pp. 2997-3003, Vol. 165.
47	OHGA, E., <i>et al.</i> , "Activin receptors are expressed on human lung fibroblast and activin A facilitates fibroblast-mediated collagen gel contraction," <i>Life Sciences</i> , 2000, pp. 1603-1613, Vol. 66.
48	OHGA, E., <i>et al.</i> , "Effects of Activin A on Proliferation and Differentiation of Human Lung Fibroblasts," <i>Biochemical and Biophysical Research Communications</i> , 1996, pp. 391-396, Vol. 228(2).

Examiner Signature	Date Considered
--------------------	-----------------

*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute for form 1449/PTO (Revised 04/2003)				Complete if Known	
				Application Number	10/755,545
				Filing Date	1/12/04
				First Named Inventor	Phillips
				Group Art Unit	1646
				Examiner Name	To Be Assigned
Sheet	5	of	7	Attorney Docket Number	048501/273281

U. S. PATENT DOCUMENTS					
	49	OKUNO, M., <i>et al.</i> , "Prevention of Rat Hepatic Fibrosis by the Protease Inhibitor, Camostat Mesilate, via Reduced Generation of Active TGF- β ," <i>Gastroenterology</i> , 2001, pp. 1784-1800, Vol. 120(7).			
	50	PATELLA, S., <i>et al.</i> , "Characterization of serum activin-A and follistatin and their relation to virological and histological determinants in chronic viral hepatitis," <i>J. Hepatol.</i> , 2001, pp. 576-583, Vol. 34(4).			
	51	PHILLIPS, D.J., <i>et al.</i> , "A sensitive and specific <i>in vitro</i> bioassay for activin using a mouse plasmacytoma cell line, MPC-11," <i>J. Endocrin.</i> , 1999, pp. 111-116, Vol. 162(1).			
	52	PHILLIPS, D.J., <i>et al.</i> , "Follistatin has a biphasic response but follicle-stimulating hormone is unchanged during an inflammatory episode in growing lambs," <i>J. Endocrin.</i> , 1998, pp. 77-82, Vol. 156.			
	53	PHILLIPS, D.J., and DE KRETSER, D.M., "Follistatin: a multifunctional regulatory protein," <i>Frontiers in Neuroendocrinology</i> , 1998, pp. 287-322, Vol. 19.			
	54	PIANKO, S., <i>et al.</i> , "Hepatocyte apoptosis is increased in chronic HCV infection and alcohol use," Abstract from Annual Meeting of American Gastroenterological Association and American Association for the Study of Liver Diseases, 11-14 May 1997.			
	55	PINZANI, M., <i>et al.</i> , "Transforming growth factor- β 1 regulates platelet-derived growth factor receptor β subunit in human liver fat-storing cells," <i>Hepatology</i> , 1995, pp. 232-239, Vol. 21(1).			
	56	PIRISI, M., <i>et al.</i> , "Evaluation of circulating activin-A as a serum marker of hepatocellular carcinoma," <i>Cancer Detect & Prev.</i> , 2000, pp. 150-155, Vol. 24(2).			
	57	QI, Z., <i>et al.</i> , "Blockade of type β transforming growth factor signaling prevents liver fibrosis and dysfunction in the rat," <i>PNAS</i> , 1999, pp. 2345-2349, Vol. 96.			
	58	RAMM, G.A., <i>et al.</i> , "Vitamin A-poor lipocytes: a novel desmin-negative lipocyte subpopulation, which can be activated to myofibroblasts," <i>Am. J. Physiol.</i> , 1995, pp. G532-41, Vol. 269(4 Pt 1).			
	59	REIMANN, T., <i>et al.</i> , "Transforming growth factor- β 1 induces activation of Ras, Raf-1, MEK and MAPK in rat hepatic stellate cells," <i>FEBS Lett.</i> , 1997, pp. 57-60, Vol. 403(1).			
	60	RITVOS, O., <i>et al.</i> , "Activin disrupts epithelial branching morphogenesis in developing glandular organs of the mouse," <i>Mech. & Devel.</i> , 1995, pp. 229-245, Vol. 50.			
	61	ROSENBAUM, J., <i>et al.</i> , "Fibroblast growth factor 2 and transforming growth factor β 1 interactions in human liver myofibroblasts," <i>Gastroenterology</i> , 1995, pp. 1986-1996, Vol. 109(6).			

Examiner Signature		Date Considered	
--------------------	--	-----------------	--

*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Use as many sheets as necessary)

Sheet

6

of

7

Complete if Known

Application Number	10/755,545
Filing Date	1/12/04
First Named Inventor	Phillips
Group Art Unit	1646
Examiner Name	To Be Assigned
Attorney Docket Number	048501/273281

U. S. PATENT DOCUMENTS

62	SAKAMOTO, Y., <i>et al.</i> , "Determination of free follistatin levels in sera of normal subjects and patients with various diseases," <i>Eur. J. Endocrinol.</i> , 1996, pp. 345-351, Vol. 135(3).
63	SAKURAI, T.A., <i>et al.</i> , "Activin A stimulates mitogenesis in Swiss 3T3 fibroblasts without activation of mitogen-activated protein kinases," <i>J. Biol. Chem.</i> , 1994, pp. 14118-14122, Vol. 269.
64	SCHWALL, R.H., <i>et al.</i> , "Activin induces cell death in hepatocytes <i>in vivo</i> and <i>in vitro</i> ," <i>Hepatology</i> , 1993, pp. 347-356, Vol. 18(2).
65	SUGIYAMA, M., <i>et al.</i> , "Expression of activin A is increased in cirrhotic and fibrotic rat livers," <i>Gastroenterology</i> , 1998, pp. 550-558, Vol. 114(3).
66	TAKABE, K., <i>et al.</i> , "Recombinant adenovirus vector encoding follistatin: A potential tool to stimulate liver regeneration," AASLD Abstract No. 351 from <i>Hepatology</i> , October 1999.
67	THOMAS, T.Z. <i>et al.</i> , "Inhibins, activins, and follistatins: Expression of mRNAs and cellular localization in tissues from men with benign prostatic hyperplasia," <i>The Prostate</i> , 1998, pp. 34-43, Vol. 34(1).
68	"Ulcerative Colitis," From National Institute of Diabetes and Digestive and Kidney Diseases (NIH Publication No. 95-1597, April 1992).
69	WANG, E.Y., <i>et al.</i> , "Identification of naturally occurring follistatin complexes in human biological fluids," <i>Biol. Reprod.</i> , 1999, pp. 8-13, Vol. 60.
70	WEBSITE: "Facts about pulmonary fibrosis and interstitial lung disease," American Lung Association website, originally www.lungusa.org/diseases/pulmfibrosis on 7 November 2000 – enclosed version downloaded from http://209.208.158.222/diseases/pulmfibrosis.html on 1 July 2004.
71	WEBSITE: NADEL, M., "Crohn's Disease (Granulomatous Ileitis and Colitis)", Internet site: http://155.37.5.42/TMGEN/67062160.htm on 6 December 2000 (enclosed copy downloaded on 25 June 2004).
72	YASUDA, H., <i>et al.</i> , "Activin A: An autocrine inhibitor of initiation of DNA synthesis in rat hepatocytes," <i>J. Clin. Invest.</i> , 1993, pp. 1491-1496, Vol. 92(3).
73	YASUDA, H., <i>et al.</i> , "Antifibrogenic effect of a deletion variant of hepatocyte growth factor on liver fibrosis in rats," <i>Hepatology</i> , 1996, pp. 636-642, Vol. 24(3).
74	YUEN, M.F., <i>et al.</i> , "Transforming growth factor- β 1, activin and follistatin in patients with hepatocellular carcinoma and patients with alcoholic cirrhosis," <i>Scand. J. Gastroenterol.</i> , 2002, pp. 233-238, Vol. 37(2).

Examiner Signature	Date Considered
--------------------	-----------------

*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute for form 1449/PTO
(Revised 04/2003)

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Use as many sheets as necessary)

Sheet

7

of

7

Complete if Known

Application Number	10/755,545
Filing Date	1/12/04
First Named Inventor	Phillips
Group Art Unit	1646
Examiner Name	To Be Assigned
Attorney Docket Number	048501/273281

U. S. PATENT DOCUMENTS

75

ZHU, J., *et al.*, "Rapamycin inhibits hepatic stellate cell proliferation in vitro and limits fibrogenesis in an *in vivo* model of liver fibrosis," *Gastroenterology*, 1999, pp. 1198-1204, Vol. 117(5).

RTA01/2161244v1

Examiner Signature		Date Considered	
-----------------------	--	--------------------	--

*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.